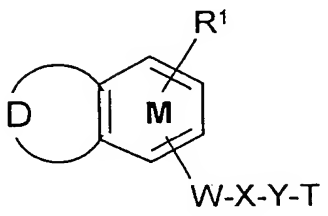
Patent Claims

1. Compounds of the formula I



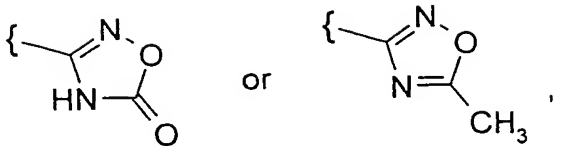
I

in which

D is absent or
is a saturated, fully or partially unsaturated 3- to 4-membered alkylene chain, in which from 1 to 3 carbon atoms may be replaced by N and/or 1 or 2 carbon atoms may be replaced by 1 or 2 O and/or 1 or 2 S atoms, but where at most up to 3 carbon atoms are replaced and where, in addition, the alkylene chain and/or a nitrogen present therein may be monosubstituted, disubstituted or trisubstituted by Hal, A, $-[C(R^3)_2]_n$-Ar, $-[C(R^3)_2]_n$-Het, $-[C(R^3)_2]_n$-cycloalkyl, OR^2, $N(R^2)_2$, NO_2, CN, $COOR^2$, $CON(R^2)_2$, NR^2COA, NR^2SO_2A, COR^2, SO_2NR^2 and/or $S(O)_mA$, and where, furthermore, one CH_2 group in the alkylene chain may also be replaced by a C=O group,

M is a phenyl ring or an aromatic heterocyclic ring, which may contain 1-2 N, O and/or S atoms,

R^1 is H, Hal, A, OR^2, $N(R^2)_2$, NO_2, CN, $COOR^2$, $CON(R^2)_2$, $-[C(R^3)_2]_n$-Ar, $-[C(R^3)_2]_n$-Het, $-[C(R^3)_2]_n$-cycloalkyl, $-[C(R^3)_2]_n-N(R^3)_2$, CN, $-C(=NH)-NH_2$ which is unsubstituted or monosubstituted by $C(=O)R^3$, $COOR^3$, OR^3 or by a conventional amino-protecting group, or



	R^2	is H, A, -$[C(R^3)_2]_n$-Ar, -$[C(R^3)_2]_n$-Het, -$[C(R^3)_2]_n$-cycloalkyl, -$[C(R^3)_2]_n$-$N(R^3)_2$ or -$[C(R^3)_2]_n$-OR^3,
	$R^{2'}$	is H, A, -$[C(R^3)_2]_n$-Ar', -$[C(R^3)_2]_n$-Het', -$[C(R^3)_2]_n$-cycloalkyl, -$[C(R^3)_2]_n$-$N(R^3)_2$ or -$[C(R^3)_2]_n$-OR^3,
	$R^{2''}$	is H, A, -$[C(R^3)_2]_n$-Ar', -$[C(R^3)_2]_n$-cycloalkyl, -$[C(R^3)_2]_n$-$N(R^3)_2$ or -$[C(R^3)_2]_n$-OR^3,
	R^3	is H or A,
	W	is -$C(R^2)_2$-, -$[C(R^2)_2]_2$-, -$OC(R^2)_2$-, -$NR^2C(R^2)_2$-, -NR^2CO- or -$CONR^2$-,
	X	is $CONR^2$, $CONR^2C(R^3)_2$, -$C(R^3)_2NR^2$, -$C(R^3)_2NR^2C(R^3)_2$, -$C(R^3)_2O$- or -$C(R^3)_2OC(R^3)_2$-,
	Y	is alkylene, cycloalkylene, Het-diyl or Ar-diyl,
	T	is a monocyclic or bicyclic, saturated, unsaturated or aromatic carbocyclic or heterocyclic ring having from 1 to 4 N, O and/or S atoms which is monosubstituted or disubstituted by =S, $=NR^2$, $=NOR^2$, $=NCOR^2$, $=NCOOR^2$ or $=NOCOR^2$ and may furthermore be monosubstituted, disubstituted or trisubstituted by Hal, A, -$[C(R^3)_2]_n$-Ar, -$[C(R^3)_2]_n$-Het, -$[C(R^3)_2]_n$-cycloalkyl, OR^3, $N(R^3)_2$, NO_2, CN, $COOR^2$, $CON(R^2)_2$, NR^2COA, $NR^2CON(R^2)_2$, NR^2SO_2A, COR^2, SO_2NR^2 and/or $S(O)_mA$,
	A	is unbranched or branched alkyl having 1-10 carbon atoms, in which one or two CH_2 groups may be replaced by O or S atoms and/or by -CH=CH- groups, and/or in addition 1-7 H atoms may be replaced by F,
	Ar	is phenyl, naphthyl or biphenyl, each of which is unsubstituted or monosubstituted, disubstituted or trisubstituted by Hal, A,

OR^3, $N(R^3)_2$, NO_2, CN, $COOR^3$, $CON(R^3)_2$, NR^3COA, $NR^3CON(R^3)_2$, NR^3SO_2A, COR^3, $SO_2N(R^3)_2$, $S(O)_mA$, $-[C(R^3)_2]_n-COOR^{2'}$ or $-O-[C(R^3)_2]_o-COOR^{2'}$,

Ar' is phenyl or benzyl, each of which is unsubstituted or mono- substituted or disubstituted by Hal or A,

Het is a monocyclic or bicyclic, saturated, unsaturated or aromatic heterocyclic ring having from 1 to 4 N, O and/or S atoms, which may be unsubstituted or monosubstituted, disubstituted or trisubstituted by carbonyl oxygen, =S, $=N(R^3)_2$, Hal, A, $-[C(R^3)_2]_n-Ar$, $-[C(R^3)_2]_n-Het^1$, $-[C(R^3)_2]_n-$cycloalkyl, $-[C(R^3)_2]_n-OR^{2'}$, $-[C(R^3)_2]_n-N(R^{2'})_2$, NO_2, CN, $-[C(R^3)_2]_n-COOR^{2'}$, $-[C(R^3)_2]_n-CON(R^{2'})_2$, $-[C(R^3)_2]_n-NR^{2'}COA$, $NR^{2'}CON(R^{2'})_2$, $-[C(R^3)_2]_n-NR^{2'}SO_2A$, $COR^{2'}$, $SO_2NR^{2'}$ and/or $S(O)_mA$,

Het^1 is a monocyclic or bicyclic, saturated, unsaturated or aromatic heterocyclic ring having 1 or 2 N, O and/or S atoms, which may be unsubstituted or monosubstituted or disubstituted by carbonyl oxygen, =S, $=N(R^3)_2$, Hal, A, $OR^{2''}$, $N(R^{2''})_2$, NO_2, CN, $COOR^{2''}$, $CON(R^{2''})_2$, $NR^{2''}COA$, $NR^{2''}CON(R^{2''})_2$, $NR^{2''}SO_2A$, $COR^{2''}$, $SO_2NR^{2''}$ and/or $S(O)_mA$,

Hal is F, Cl, Br or I,

n is 0, 1 or 2,

m is 0, 1 or 2,

o is 1, 2 or 3,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

2. Compounds according to Claim 1, in which

D is absent,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

3. Compounds according to Claim 1 or 2, in which

M is a phenyl ring,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compounds according to Claim 1 or 3, in which

D is a saturated, fully or partially unsaturated 3- to 4-membered alkylene chain, in which from 1 to 3 carbon atoms may be replaced by N and/or 1 or 2 carbon atoms may be replaced by 1 or 2 O and/or 1 or 2 S atoms, but where at most up to 3 carbon atoms are replaced and where, in addition, the alkylene chain and/or a nitrogen present therein may be monosubstituted, disubstituted or trisubstituted by Hal, A, OR^2 or $N(R^2)_2$, and where, furthermore, one CH_2 group in the alkylene chain may also be replaced by a C=O group,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

5. Compounds according to Claim 1, 3 or 4, in which

D is a saturated, fully or partially unsaturated 3- to 4-membered alkylene chain, in which from 1 to 3 carbon atoms may be replaced by N and/or 1 or 2 carbon atoms may be replaced by 1 or 2 O and/or 1 or 2 S atoms, but where at most up to 3 carbon atoms are replaced and where, in addition, the alkylene chain and/or a nitrogen present therein may be monosubstituted, disubstituted or trisubstituted by A or NH_2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

6. Compounds according to Claim 1, 3, 4 or 5, in which

D is -CO-NH-CO, -CO-NH-CH_2-, -NH-CH=CH-, -O-CH=CH-, -N=CH-O-, -N=CH-NH-, -NH-NH-CO-, -NH-N=N-,

-NH-CO-CH_2-, -NH-CO-O-, -N=CH-S-, -NH-CO-S-, -NH-CO-NH-, -NH-N=CH-, -S-N=CH-, =C-S-N=, -O-N=CH-, -O-NH-CO-, -NH-O-CO-, -N=CH-CH=CH-, -CH=N-CH=CH-, -N=N-CH=CH-, -N=CH-N=CH-, -N=CH-CH=N-, -N=N-N=CH-, -NH-CO-CH=CH-, -NH-CH=CH-CO-, -NH-CO-CH_2-CH_2-, -NH-CH_2-CH_2-CO-, -NH-CO-N=CH-, -N=CH-NH-CO-, -NH-CO-NH-CO-, -NH-CO-NH-CH_2-, -CH=N-N=CH-, -N^--S^+=-N-, -O-CH_2-O-, -CH=N-NH-CO-, -CH=CH-NH-, -NH-N=CH-, -O-CH_2CH_2-O-, -CO-NH-NH-CO-, -N=N-NH-CO-, -O-CO-NH-CH_2-, -O-CO-NH-CO- or -CH_2-CH_2-CH_2-CH_2-,

and where, in addition, the alkylene chain and/or a nitrogen present therein may be monosubstituted, disubstituted or trisubstituted by A or NH_2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

7. Compounds according to Claim 1, 3, 4, 5 or 6,

in which

D is -CH=N-CH=CH-, -NH-N=CH-, -O-N=CH- or -CH_2-CH_2-CH_2-CH_2-,

and where, in addition, D may be monosubstituted by NH_2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

8. Compounds according to Claim 1,

in which

D is absent or

is -CH=N-CH=CH-, -NH-N=CH-, -O-N=CH- or -CH_2-CH_2-CH_2-CH_2-,

and where, if D is present, D may additionally be monosubstituted by NH_2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

9. Compounds according to one or more of Claims 1-8, in which

R^1 is H or $-[C(R^3)_2]_n-N(R^3)_2$,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

10. Compounds according to one or more of Claims 1-9, in which

W is $-OC(R^2)_2-$ or $-NR^2C(R^2)_2-$,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

11. Compounds according to one or more of Claims 1-10, in which

W is $-OC(R^{2a})_2-$ or $-NR^2C(R^{2a})_2-$,

R^{2a} is H, A' or Ar',

A' is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, in which 1-7 H atoms may be replaced by F, and

Ar' is phenyl or benzyl, each of which is unsubstituted or monosubstituted or disubstituted by Hal,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

12. Compounds according to one or more of Claims 1-11, in which

X is CONH,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

13. Compounds according to one or more of Claims 1-12, in which

Y is Ar-diyl,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

14. Compounds according to one or more of Claims 1-13, in which

Y is phenylene which is unsubstituted or monosubstituted or disubstituted by A, Cl or F,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

15. Compounds according to one or more of Claims 1-14, in which

T is a monocyclic or bicyclic, saturated, unsaturated or aromatic carbocyclic or heterocyclic ring having 1 or 2 N and/or O atoms which is monosubstituted or disubstituted by =S, $=NR^2$, $=NOR^2$, $=NCOR^2$, $=NCOOR^2$ or $=NOCOR^2$ and may furthermore be monosubstituted or disubstituted by Hal or A,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

16. Compounds according to one or more of Claims 1-15, in which

T is a monocyclic or bicyclic, saturated or unsaturated heterocyclic ring having 1 or 2 N and/or O atoms which is monosubstituted or disubstituted by $=NR^2$, =S or $=NOR^2$,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

17. Compounds according to one or more of Claims 1-16,

in which

T is piperidin-1-yl, pyrrolidin-1-yl, 1*H*-pyridin-1-yl, morpholin-4-yl, piperazin-1-yl, 1,3-oxazolidin-3-yl, 2*H*-pyridazin-2-yl, azepan-1-yl or 2-azabicyclo[2.2.2]octan-2-yl, each of which is monosubstituted or disubstituted by $=NR^2$, =S or $=NOR^2$,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

18. Compounds according to one or more of Claims 1-17, in which

T is piperidin-1-yl, pyrrolidin-1-yl, 1*H*-pyridin-1-yl, morpholin-4-yl, piperazin-1-yl, 1,3-oxazolidin-3-yl, 2*H*-pyridazin-2-yl, azepan-1-yl or 2-azabicyclo[2.2.2]octan-2-yl, each of which is monosubstituted or disubstituted by $=NR^{2b}$, =S or $=NOR^{2b}$,

R^{2b} is H, $-CH_2CH_2NA'_2$, OH or OA',

A' is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, in which 1-7 H atoms may be replaced by F,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

19. Compounds according to one or more of Claims 1-18, in which

T is piperidin-1-yl, pyrrolidin-1-yl, 1*H*-pyridin-1-yl, morpholin-4-yl, piperazin-1-yl, 1,3-oxazolidin-3-yl, 2*H*-pyridazin-2-yl, azepan-1-yl or 2-azabicyclo[2.2.2]octan-2-yl, each of which is monosubstituted by $=NR^{2b}$ or $=NOR^{2b}$,

R^{2b} is H, $-CH_2CH_2NA'_2$, OH or OA",

A" is methyl, ethyl, propyl, isopropyl or butyl,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

20. Compounds according to one or more of Claims 1-19, in which

D is absent or
is -CH=N-CH=CH-, -NH-N=CH-, -O-N=CH- or
$-CH_2-CH_2-CH_2-CH_2-$,
and where, if D is present, D may additionally be monosubstituted by NH_2,

M is a phenyl ring,

R^1 is H or CH_2NH_2,

W is $-OC(R^{2a})_2-$ or $-NR^2C(R^{2a})_2-$,

R^{2a} is H, A' or Ar',

A' is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, in which 1-7 H atoms may be replaced by F, and

Ar' is phenyl or benzyl, each of which is unsubstituted or monosubstituted or disubstituted by Hal,

X is CONH,

Y is phenylene which is unsubstituted or monosubstituted or disubstituted by A, Cl or F,

T is piperidin-1-yl, pyrrolidin-1-yl, 1*H*-pyridin-1-yl, morpholin-4-yl, piperazin-1-yl, 1,3-oxazolidin-3-yl, 2*H*-pyridazin-2-yl, azepan-1-yl or 2-azabicyclo[2.2.2]octan-2-yl, each of which is monosubstituted by $=NR^{2b}$, S or $= NOR^{2b}$,

R^{2b} is H, $-CH_2CH_2NA'_2$, OH or OA",

A" is methyl, ethyl, propyl, isopropyl or butyl,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

21. Compounds according to Claim 1, selected from the group consisting of

2-(3-aminomethylphenylamino)-*N*-[3-chloro-4-(2-hydroxyiminopyrrolidin-1-yl)phenyl]-2-phenylacetamide;

2-(3-aminomethylphenylamino)-*N*-[3-chloro-4-(2-imino-pyrrolidin-1-yl)phenyl]-2-phenylacetamide;

2-(1-aminoisoquinolin-7-yloxy)-*N*-[4-(2-methoxyimino-piperidin-1-yl)phenyl]-4-methylvaleramide;

2-(1-aminoisoquinolin-7-yloxy)-*N*-[4-(2-iminopiperidin-1-yl)-phenyl]-4-methylvaleramide;

2-(3-aminomethylphenylamino)-*N*-[3-methyl-4-(2-hydroxy-iminopiperidin-1-yl)phenyl]-2-(2-fluorophenyl)acetamide;

2-(3-aminomethylphenylamino)-*N*-[3-methyl-4-(2-imino-piperidin-1-yl)phenyl]-2-(2-fluorophenyl)acetamide;

2-(3-aminomethylphenylamino)-*N*-[3-chloro-4-(2-hydroxy-iminopyrrolidin-1-yl)phenyl]-2-(2-fluorophenyl)acetamide;

2-(3-aminomethylphenylamino)-*N*-[3-chloro-4-(2-imino-pyrrolidin-1-yl)phenyl]-2-(2-fluorophenyl)acetamide;

2-(1-aminoisoquinolin-7-yloxy)-*N*-[3-methyl-4-(2-imino-piperidin-1-yl)phenyl]-4-methylvaleramide;

2-(3-aminomethylphenylamino)-*N*-[3-trifluoromethyl-4-(2-aza-bicyclo[2.2.2]octan-3-imino-2-yl)phenyl]-2-(2-fluorophenyl)acetamide;

2-(3-aminomethylphenylamino)-*N*-[3-trifluoromethyl-4-(2-aza-bicyclo[2.2.2]octan-3-hydroxyimino-2-yl)phenyl]-2-(2-fluorophenyl)-acetamide;

2-(1-aminoisoquinolin-7-yloxy)-*N*-[3-methyl-4-(2-methoxy-iminopiperidin-1-yl)phenyl]-4-methylvaleramide;

2-(3-aminomethylphenylamino)-*N*-[3-fluoro-4-(2-imino-pyrrolidin-1-yl)phenyl]-2-(2-chlorophenyl)acetamide;

2-(3-aminomethylphenylamino)-*N*-[3-methyl-4-(2-imino-pyrrolidin-1-yl)phenyl]-2-(2-fluorophenyl)acetamide;

2-(3-aminomethylphenylamino)-*N*-[3-chloro-4-(2-imino-pyrrolidin-1-yl)phenyl]-2-(2-chlorophenyl)acetamide;

2-(3-aminobenzo[d]isoxazol-5-ylamino)-*N*-[3-chloro-4-(2-iminopyrrolidin-1-yl)phenyl]-2-phenylacetamide;

2-(1-aminoisoquinolin-7-yloxy)-*N*-[4-(2-iminopyrrolidin-1-yl)-phenyl]-4-methylvaleramide;

2-(1-aminoisoquinolin-7-yloxy)-*N*-[4-(2-methoxyimino-pyrrolidin-1-yl)phenyl]-4-methylvaleramide;

2-(3-aminomethylphenylamino)-N-[3-methyl-4-(2-(2-dimethyl-aminoethylimino)pyrrolidin-1-yl)phenyl]-2-(2-chloro)phenyl-acetamide;

2-(5-amino-5,6,7,8-tetrahydronaphthalen-2-yloxy)-*N*-[4-(3-imino-2-azabicyclo[2.2.2]oct-2-yl)-3-methylphenyl]-2-phenyl-acetamide;

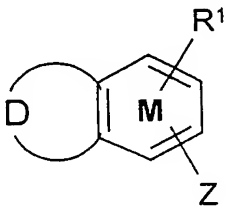
2-(5-amino-5,6,7,8-tetrahydronaphthalen-2-yloxy)-2-(2-fluoro-phenyl)-*N*-[4-(3-imino-2-azabicyclo[2.2.2]oct-2-yl)-3-methylphenyl]-acetamide;

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

22. Process for the preparation of compounds of the formula I according to Claims 1-21 and pharmaceutically usable derivatives, solvates and stereoisomers thereof, characterised in that

a) for the preparation of a compound of the formula I in which W is $-OC(R^2)_2-$ or $-NR^2C(R^2)_2-$,

a compound of the formula II



II

in which

Z is OH or NHR^2,
and R^1, R^2, D and M are as defined in Claim 1,
with the proviso that any further OH and/or amino group present is protected,

is reacted with a compound of the formula III

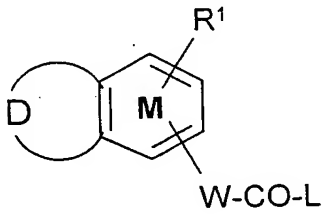
$$L\text{-}C(R^2)_2\text{-}X\text{-}Y\text{-}T \qquad III$$

in which
L is Cl, Br or I, and R^2, X, Y and T are as defined in Claim 1,

and any protecting group is subsequently removed,

b) for the preparation of a compound of the formula I
in which X is $CONR^2$ or $CONR^2C(R^3)_2$,

a compound of the formula IV



IV

in which
L is Cl, Br, I or a free or reactively functionally modified OH group,
and R^1, D, M and W are as defined in Claim 1,
with the proviso that any further OH and/or amino group present is protected,

is reacted with a compound of the formula V

Z'-Y-T V

in which
Z' is NHR^2 or $NHR^2C(R^3)_2$,
and R^2, Y and T are as defined in Claim 1,
and any protecting group is subsequently removed,

c) and/or in that a radical T and/or R^1 in a compound of the formula I is converted into another radical T and/or R^1

by, for example,

i) converting a sulfanyl compound into an imino compound,
ii) removing an amino-protecting group,

and/or
a base or acid of the formula I is converted into one of its salts.

23. Compounds of the formula I according to one or more of Claims 1 to 21 as inhibitors of coagulation factor Xa.

24. Compounds of the formula I according to one or more of Claims 1 to 21 as inhibitors of coagulation factor VIIa.

25. Medicament comprising at least one compound of the formula I according to one or more of Claims 1 to 21 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.

26. Medicament comprising at least one compound of the formula I according to one or more of Claims 1 to 21 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active ingredient.

27. Use of compounds according to one or more of Claims 1 to 21 and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of thromboses, myocardial infarction, arteriosclerosis, inflammation, apoplexia, angina pectoris, restenosis after angioplasty, claudicatio intermittens, migraine, tumours, tumour diseases and/or tumour metastases.

28. Set (kit) consisting of separate packs of

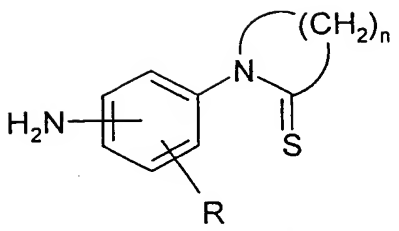
(a) an effective amount of a compound of the formula I according to one or more of claims 1 to 21 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios,

and

(b) an effective amount of a further medicament active ingredient.

29. Use of compounds of the formula I according to one or more of Claims 1 to 21 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, for the preparation of a medicament for the treatment of thromboses, myocardial infarction, arteriosclerosis, inflammation, apoplexia, angina pectoris, restenosis after angioplasty, claudicatio intermittens, migraine, tumours, tumour diseases and/or tumour metastases, in combination with at least one further medicament active ingredient.

30. Intermediates of the formula VI



VI

in which

R is H, F, Cl or A',

A' is alkyl having 1-6 carbon atoms, in which 1-7 H atoms may be replaced by F,

n is 3, 4 or 5,

and salts thereof.